

IN THE SPECIFICATION:

Please amend as follows:

At page 1, line 5, please insert the following paragraph:

RELATED APPLICATIONS

The present application is a continuation-in-part of copending application Serial No. 09/668,508, filed September 22, 2000, which in turn is a continuation-in-part of copending application Serial No. 09/404,895, filed September 24, 1999, to each of which the instant application claims the benefit of the filing date pursuant to 35 U.S.C. § 120, and each of which is incorporated herein by reference in its entirety.

Please replace the paragraphs starting on page 113, line 5 and continuing to page 114, line 16 with the following paragraphs.

When grown in medium alone, the secondary cultures maintain a stellate morphology and do not differentiate (FIGURE 7A). Differentiation must be stimulated by an exogenous agent and dexamethasone is used to accomplish this. In this system dexamethasone acts as a non-specific differentiating agent. Although its exact mechanism of action is unknown, dexamethasone has been used in a number of culture systems to stimulate differentiation of stem cells (Ball and Sanwal, 1980; Owen and Joyner, 1987; Bellows et al., 1990; Greenberger, 1979; Houner et al, 1987; Schiwek and Loffler, 1987; Bernier and Goltzman, 1993; Zimmerman and Cristae, 1993; Grigoriadis et al., 1989; and Guerriero and Florini, 1980).

Cells in the secondary cultures treated with dexamethasone differentiated into several morphologies indicative of skeletal muscle myotubes, chondrocytes, osteoblasts, adipocytes, smooth muscle cells, endothelial cells, and fibroblasts. Phenotypic confirmation was obtained by immunochemical, histochemical, or functional LDL-uptake techniques designed to identify particular phenotypic expression markers for the particular differentiated cells.

The timing of the appearance of the particular phenotypes and the particular concentration of dexamethasone used to elicit these responses in this study were identical to those conditions for mesenchymal stem cells isolated from embryonic chick (Young et al., 1992a), embryonic rat periosteum (Grigoriadis et al., 1988), neonatal rat skeletal muscle (Lucas et al., 1995), neonatal rat heart (Warejcka et al., 1996), and adult rabbit skeletal muscle (Pate et al., 1993). The cells isolated in this study from rat granulation tissue appear to behave identically in culture to populations of MSCs present in other connective tissues. It therefore seems likely that the cells in this study are a population of MSCs.

Theoretically, this population of MSCs may be composed of two subpopulations: 1) progenitor stem cells for each of the phenotypes observed and/or 2) lineage uncommitted pluripotent stem cells. Previous examples of the existence of lineage-committed progenitor stem cell populations include the unipotent progenitor myosatellite stem cell of skeletal muscle (Mauro, 1961; Snow, 1978; Grounds, 1990, 1991), the unipotent progenitor chondrogenic and osteogenic stem cells of the perichondrium and periosteum, respectively (Bloom and Fawcett, 1994), and the bipotent progenitor chondrogenic, osteogenic stem cells in marrow (Owen, 1988; Beresford, 1989). The existence of lineage-uncommitted pluripotent MSCs is based on the results from clonally isolated stem cells. Individual clonal cell lines derived from embryonic rat periosteum (Grigoriadis, 1988) and embryonic chick skeletal muscle, dermis, and heart (Young et al., 1993) have demonstrated multiple phenotypes when treated with dexamethasone, suggesting the existence of lineage-uncommitted pluripotent stem cells in these tissues. In addition, preliminary data from clonal cell lines generated from cells isolated from neonatal rat skeletal muscle have also shown individual clones that can differentiate into multiple mesodermal phenotypes (Davis et al., 1995), suggesting continuance of pluripotent stem cells into post-partum life.

At page 234, line 4 please delete the text on this line as follows:

ABSTRACT

At page 255, line 30 please delete the text on this line as follows:

ABSTRACT

At page 274, line 2 please delete the text on this line as follows:

ABSTRACT